REMARKS

Claims 32-34, 51, 78, 82-87, 89, 90, 93 and 94 are pending in the application with claims 51, 78, 82-87, 89, 90, 93 and 94 under examination. Applicants acknowledge that the rejections of claims 51 and 94 under 35 U.S.C. § 112, second paragraph, as being indefinite; claims 78-80 and 82-95 under 35 U.S.C. § 112, first paragraph, for lacking enablement; claims 78-81, 82-92, 94 and 95 and claims 83-93 under 35 U.S.C. § 112, first paragraph, for lacking written description, and the rejection of claims 83-87 and 91-93 under 35 U.S.C. § 102(e) as being anticipated by Venter et al. (U.S. Pat. No. 6,821,339), have been withdrawn. Accordingly, only a single ground of rejection remains, which Applicant responds to below.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 51, 78, 82-87, 89, 90, 93 and 94 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement. The Office alleges that "[t]he rejection is based on the fact that the specification fails to demonstrate a link between myosin I gene expression levels, either protein or mRNA expression, and any type of cancer." Applicants respectfully disagree.

Applicants respectfully submit that the application provides a sufficient link between the claimed SEQ ID NO:777 and diagnosis of cancer to enable those skilled in the art to practice the invention as claimed. As described in Applicants' previous response, the application teaches the use of oncogenic retroviruses for the identification of host cancer related sequences such as the claimed SEQ ID NO:777. With respect to the assertion that the specification fails to demonstrate a link, the application teaches:

> The present invention is directed to a number of sequences associated with cancers, especially lymphoma, breast cancer or prostate cancer. **The relatively tight linkage between clonally-integrated proviruses and protooncogenes forms "provirus tagging"**, in which slow-transforming retroviruses that act by an insertion mutation mechanism are used to isolate protooncogenes. In some models, uninfected animals have low cancer rates, and infected animals have high cancer rates. It is known that many of the retroviruses involved do not carry transduced host protooncogenes or pathogenic trans-acting viral genes, and thus the cancer incidence must therefore be a direct consequence of proviral integration effects into host protooncogenes. Since proviral integration is random, rare integrants will "activate" host protooncogenes that provide a selective growth

> advantage, and these rare events result in new proviruses at clonal stoichiometres in tumors. In contrast to mutations caused by chemicals, radiation, or spontaneous errors, protooncogene insertion mutations can be easily located by virtue of the fact that a convenient-sized genetic marker of known sequence (the provirus) is present at the site of mutation. Host sequences that flank clonally integrated proviruses can be cloned using a variety of strategies. Once these sequences are in hand, the tagged protooncogenes can be subsequently identified. **The presence of provirus at the same locus in two or more independent tumors is *prima facie* evidence that a protooncogene is present at or very near the provirus integration sites. This is because the genome is too large for random integrations to result in observable clustering. Any clustering that is detected is unequivocal evidence for biological selection (i.e. the tumor phenotype).** Moreover, the pattern of proviral integrants (including orientations) provides compelling positional information that makes localization of the target gene at each cluster relatively simple. The three mammalian retroviruses that are known to cause cancer by an insertion mutation mechanism are FeLV (leukemia/lymphoma in cats), MLV (leukemia/lymphoma in mice and rats), and MMTV (mammary cancer in mice).
>
> **Thus, the use of oncogenic retroviruses, whose sequences insert into the genome of the host organism resulting in cancer, allows the identification of host sequences involved in cancer.** These sequences may then be used in a number of different ways, including diagnosis, prognosis, screening for modulators (including both agonists and antagonists), antibody generation (for immunotherapy and imaging), etc. However, as will be appreciated by those in the art, oncogenes that are identified in one type of cancer such as lymphoma or leukemia have a strong likelihood of being involved in other types of cancers as well. Thus, while the sequences outlined herein are initially identified as correlated with lymphoma, they can also be found in other types of cancers as well, outlined below.

Id. at paragraphs 0027-0028 (emphasis added; *see also* para. 0298, describing "[t]he presence of provirus at the same locus in two or more independent tumors is *prima facie* evidence that a protooncogene is present at or very near the proviral integration sites. This is because the genome is too large for random integrations to result in observable clustering. Any clustering that is detected is unequivocal evidence for biological selection during tumorigenesis.").

Based on the above teachings and guidance, those skilled in the art would understand that identification of a protooncogene by provirus tagging provides a sufficient link between the identified protooncogen and cancer. With respect to the assertion that Berns' (*Arch. Virol.* 102:1-18 (1988)) teaching that provirus tagging can uncover genes contributing to any stage of the tumorigenic process could result in dissipation of differential expression by the time a tumor

is established, it is respectfully submitted that no such teaching has been found by Applicant. Oncogenes promote tumorigenesis through overexpression of a protooncogene compared to expression levels in an unaffected individual or tissue. The identification of protooncogenes contributing to any stage of a tumorigenic process as described in Berns simply means that provirus tagging can be used to discover a protooncogene and that the discovered protooncogenes can then be used for early detection. Accordingly, in addition to Applicants' teachings and guidance provided in the application, Berns further supports enablement of the invention as claimed.

In light of the above remarks, Applicants submit that the application provides a sufficient link between the claimed SEQ ID NO:777 and the diagnosis of cancer to enable those skilled in the art to practice the invention as claimed without undue experimentation. Withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In light of the Amendments and Remarks herein, Applicant submits that the claims are in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he is invited to call the undersigned attorney.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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